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AORTIC DISSECTION AND SUDDEN DEATH- 3 CASE SCENARIOS: GENETIC BASIS

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ABSTRACT

Aortic dissection is one of the rare and fatal causes of sudden death. It is usually missed only to be revealed at autopsy. During the routine specimen collection for the thesis work 3 cases of missed aortic dissection were revealed at the autopsy in a 40yr old unmarried female,22 yr old unmarried male and a 20yr old primi gravida who succumbed to sudden death in a hospital setting. These 3 cases were studied in detail to understand the causes and genetic basis of Aortic dissection leading to sudden death.

KEYWORDS: Aortic Dissection, Sudden Death

INTRODUCTION

Out of the total number of cases coming to the Forensic department ,sudden death accounted to 10.3% .Sudden death occurred mainly due to coronary atherosclerosis and only less than 1% was found to be due to Aortic Dissection[1].Strikingly all the deaths due to aortic dissection discussed here were young adults who shared some risk factors in common. If these risk factors are screened properly the incidence of sudden death due to Aortic dissection can be brought down to a lower level.

METHODOLOGY

The present study was designed as Case series .It was done in the Dept of Forensic Medicine, Govt. Medical College, Thrissur as a part of the postgraduate thesis work within a period of 1 yr (2012 march-2013 February).

OBSERVATION

Out of the total number of deaths recorded in the Department of Forensic Medicine, Government Medical College Thrissur, Sudden death attributed to 10. 8%(Figure 1)

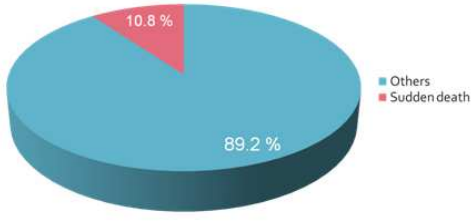

Figure 1: The Figure Shows the Percentage of Sudden Death to the Total Percentage of Deaths Reported in Forensic Department of

Government Medical College Thrissur (2012 March-2013 February)

Out of 10.8% ,sudden death due to Aortic dissection accounted to 1.5%,ie we got 3 cases of Aortic dissection among the total 20 cases. The 3 different case histories were as follows:

Case 1: A 40yr old unmarried female with history of mild mental retardation was admitted with mild epigastric pain for which she was treated with antacids. Still she continued to complain of epigastric pain and succumbed to sudden death on the very next day.

On Autopsy she was found to be moderately built & nourished. There were no obvious anomalies or signs of poisoning. On opening up of the thoracic cavity 1 litre of blood was found in the pericardial cavity from Aortic dissection starting from the root of Aorta. In addition to this Aorta showed Bicuspid Aortic valve.

Case 2: A 20yr old primi gravid a presented at 24wks to the emergency department with history of sudden onset of dyspnoea, nausea, and vomiting for 5 minutes followed by sudden death due to cardiac arrest. There was no h/o any medical illnessin the past. Antenatal history was also uneventful.

On Autopsy she was found to be well built & nourished. There were no signs of poisoning. Uterus was intact with a 24 weeks old dead fetus. On opening up of the thoracic cavity 2litres of blood was found in the left hemi thorax from Aortic dissection involving the Arch of Aorta.

Case 3: A 22yr old male was found dead in his work place. History from his relatives did not attribute the cause of death to any medical or surgical illness.

On Autopsy he was found to be moderately built & nourished. There were no signs of poisoning. On opening up of thoracic cavity 1.5 litres of blood was found in the pericardium from Aortic dissection involving Ascending Aorta. The Aorta also had Bicuspid Aortic valve.

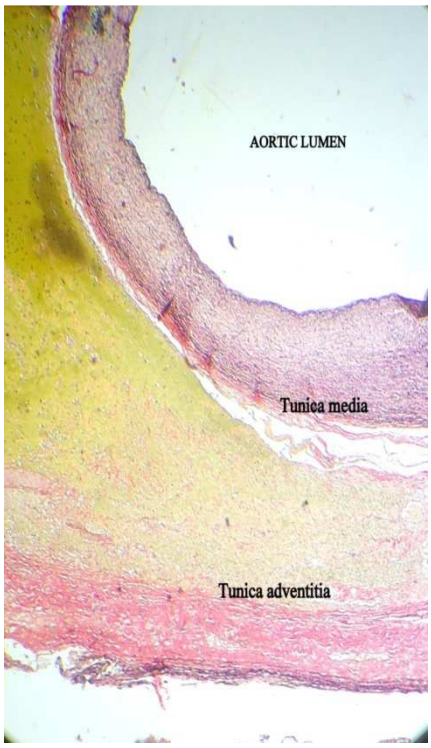

Figure 2: The Picture Shows the Plane of Aortic Dissection between

Tunica Media and Tunica Adventitia (Verhoeff's Vangieson Stain)

DISCUSSIONS

A dissection plane is created within the Tunica media extending from Tunica intima and tracking towards Tunica adventitia in all the three cases.

At the tissue level, the aorta showed cystic medial necrosis,loss of elastic fibres and altered smooth muscle cell alignment.

According to Stanford classification there are 2 types of Aortic dissections-Type A (whole Aorta ie Ascending, arch or descending) and Type B(only descending Aorta).The present cases belong to Type A of Stanford Classification.

In case 1, mental retardation and bicuspid Aortic valve were the risk factors.In case 2, pregnancy was the risk factor and in case 3, bicuspid aortic valve was the risk factor.

Males are more affected - 2:1 to 5:1(Shennan T, DeBakey ME etal).In women under 40 years, about 50% of all aortic dissections occur during pregnancy (3rd trimester)(Schnitker MA etal, Pedowitz P etal).The association of facial dysmorphism and mental retardation may lead to the diagnostic consideration of an aortic disorder (Shi-min Yuan).

The association of bicuspid aortic valve with aortic medial abnormalities("cystic medial necrosis"),the bicuspid valve increases the risk at least ninefold (Edwards WD).Echocardiographic screening of first-degree relatives of patients with BAV can be done to detect impending Aortic dissections(Huntington K).

The John Ritter Research Program has discovered a New Gene Defect Causing Thoracic Aortic Disease. Recurrent genetic mutation of gene PRKG1 has been linked to deadly thoracic aortic dissections in family members. The gene alters the function of the protein and causes the muscle cells in the wall of the aorta to respond incorrectly to pulsatile blood flow from the heart, and the change in this one protein ultimately causes thoracic aortic aneurysm and acute aortic dissection. They suffered acute aortic dissections at young ages (17 to 51 years).

Role of Genetics

20% of aortic dissections had strong association with genetic disorders like: Marfan syndrome (MfS) (20/100,000 with equal gender distribution), Loeys-Dietz syndrome (LDS), Shprintzen-Goldberg syndrome and Ehlers-Danlos syndromes (EDS)

Non-syndromic aortic dilatation associates to mutations in specific genes.Over 2400 mutations from 18 genes have been identified behind inherited dilated aortic diseases.

Some important genes associated with Aortic dissection are

Table 1: Genes Associated with Aortic Dissection

FBN1	**Fibrillin 1**
FBN2	Fibrillin 2
TGFB2	Transforming growth factor, beta 2
TGFBR1	Transforming growth factor, beta receptor 1
TGFBR2	Transforming growth factor, beta receptor 2

Familial TAAD (Thoracic Aortic Aneurysms and Dissections) is primarily inherited as an autosomal dominant trait.The majority of individuals with familial TAAD have an affected parent.The children of an affected parent have an up

to 50% chance of inheriting the genetic predisposition to TAAD.Prenatal testing for pregnancies at increased risk is possible if the disease-causing mutation in the family is known. This can be done with the help of genetic counseling.

To confirm or to establish the diagnosis in a proband there are different methods available. Multi-gene panel is one method whererall the genes that cause dissections are sequenced simultaneously. Predictive testing requires prior identification of the disease-causing mutation in the family and thereby can identify at risk family members. Prenatal diagnosis and preimplantation genetic diagnosis (PGD) can be done for at-risk pregnancies.

Utilizing efficient gene diagnostics has provided a specific gene diagnosis for over 85% of patients in a pediatric MfS population (Faivre et al. 2009).Sequencing both TGFBR1 and TGFBR2 genes can be done to find gene diagnosis in 95% of the patients with LDS. It has direct effects on follow-up and treatment decisions because aortic dissection develops in narrower aorta and at younger age in LDS compared to MfS (Van Hemelrijk et al. 2010). Family studies demonstrate that up to 19% of persons with TAAD without a known genetic syndrome have a first-degree relative with TAAD [Biddinger et al 1997, Coady et al 1999, Albornoz et al 2006].

SUMMARY

All valvular anomalies need a regular follow-up.In cases of mental retardation a detailed cardiovascular evaluation is recommended.Pregnant lady presenting with vomiting and syncope we should also think about the rarest of the rarest possibility like Aortic dissection. Strong association of risk factors like Pregnancy,Bicuspid Aortic valve and Mental Retardation should always be considered in case of Aortic dissection.

Significant advances have improved the understanding of the association of genetics and aortic aneurysmal disease. The disorders discussed above, integrate most of the proportion of the aortic disease, particularly in younger patients.

CONCLUSIONS

It’s better not to hesistate to think about the rarest possibility like Aortic dissection in an emergency case ,which may otherwise prove fatal.The isolation of new genes and their correlations with genetic syndromes do allow us not only to understand the pathophysiology involved in the genesis of the aortic aneurysm, but also pave the development of better clinical and surgical proposed treatments in affected individuals.Lets hope in the coming future with advances in the genetic field scientists may even come up with gene vaccines or antibodies which prevents mutation or even kills the gene causing the disease

REFERENCES

1. Shennan T. Dissecting aneurysms. Medical Research Council (Great Britain). Special report series. No 193, London: His majesty`s Stationery Office 13f., 1934.
2. DeBakey ME, McCollum CH, Crawford ES, Morris GC Jr, Howell J, Noon GP, LawrieG. Dissection and dissecting aneursyms of the aorta. twenty-year follow-up of five hundred twenty-seven patients treated surgically. Surgery 1982;92:1118-34.
3. Schnitker MA, Bayer CA. Dissecting aneurysm of the aorta in young individuals, particularly in association with pregnancy: with report of a case. Ann Intern Med 1944;20: 486-511.

4. Pedowitz P, Perrell A. Aneurysms complicated by pregnancy. I. Aneurysms of the aorta and ist major branches. Am J Obstet Gynecol 1957;73: 720-35.
5. Shi-min yuan .Aortic disorders, facial dysmorphism and mental retardation: clinical features and genetic conditions Acta Medica Mediterranea, 2013, 29: 817
6. Edwards WD, Leaf DS, Edwards JE. Dissecting aortic aneurysm associated with congenital bicuspid aortic valve. Circulation 1978;57:1022–5.
7. Huntington K., Hunter A.G., Chan K.L.; A prospective study to assess the frequency of familial clustering of congenital bicuspid aortic valve. J Am Coll Cardiol. 30 1997:1809-1812
8. Van Hemelrijk, C et al. The Loeys-Dietz syndrome: an update for the clinician. Current Opinion in Cardiology 2010, 25(6), 546–551
9. Caglayan, A.O. & Dundar, M. Inherited diseases and syndromes leading to aortic aneurysms and dissections.European Journal of Cardio-thoracic Surgery 2009, 35(6), 931–940
10. Ades LC, Sullivan K, Biggin A, Haan EA, Brett M, Holman KJ, Dixon J, Robertson S, Holmes AD, Rogers J, Bennetts B. FBN1, TGFBR1, and the Marfan-craniosynostosis/mental retardation disorders revisited. Am J Med Genet A. 2006;140:1047–58.
11. Albornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA, Elefteriades JA. Familial thoracic aortic aneurysms and dissections--incidence, modes of inheritance, and phenotypic patterns. Ann Thorac Surg. 2006;82:1400–5.
12. Arai T, Akiyama Y, Okabe S, Ando M, Endo M, Yuasa Y. Genomic structure of the human Smad3 gene and its infrequent alterations in colorectal cancers. Cancer Lett. 1998;122:157–63.
13. Biddinger A, Rocklin M, Coselli J, Milewicz DM. Familial thoracic aortic dilatations and dissections: a case control study. J Vasc Surg. 1997;25:506–11.
14. Booms P, Pregla R, Ney A, Barthel F, Reinhardt DP, Pletschacher A, Mundlos S, Robinson PN. RGD-containing fibrillin-1 fragments upregulate matrix metalloproteinase expression in cell culture: a potential factor in the pathogenesis of the Marfan syndrome. Hum Genet. 2005; 116:51–61.